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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,480	12/13/2004	Hudson Freeze	UCSD-08831	4479

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EXAMINER	
MACAULEY, SHERIDAN R	

ART UNIT	PAPER NUMBER
1653	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,480	FREEZE ET AL.	
	Examiner	Art Unit	
	SHERIDAN MACAULEY	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *136,144-152,154,155,157-159,162-164 and 167-176* is/are pending in the application.

4a) Of the above claim(s) *144-152,154,155,157-159 and 162-164* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *136 and 167-176* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on June 21, 2010 has been received and entered. All evidence and arguments have been fully considered. Claims 136, 144-152, 154, 155, 157-159, 162-164 and 167-176 are pending.

Response to Amendment

Applicant's response to the Notice of Non-Compliant Amendment mailed on May 25, 2010 has been received and entered. It is noted that the numbering of the claims in the non-compliant amendment filed on February 22, 2010 was revised to the appropriate claim numbering in the amendment received on June 21, 2010. Although the changes in the latter amendment are relative to the amendment dated on February 22, 2010, which was not entered, rather than the previously entered claim amendment (received on October 7, 2009), the intention of the claim markings is clear and the amendment has been entered, as is made of record in this Office action.

Election/Restrictions

1. Due to previous requirements for restriction/election, claims 144-152, 154, 155, 157-159 and 162-164 are withdrawn. Applicant's amendment to the claims on October 7, 2009 resulted in a supplemental requirement for restriction/election. In response to the requirement mailed on January 21, 2010, applicant elected the invention of Group I (claims 136 and 170-176) in the reply filed on February 22, 2010, with traverse. The traversal is on the ground(s) that the restriction is improper because it is based on a

changed form of the previously examined claims and thus there is no necessity for the new requirement for restriction/election. This argument has been found to be persuasive and the requirement for restriction mailed on January 21, 2010 is withdrawn. Claims 167-169 are therefore included with the claims under examination.

2. Claims 144-152, 154, 155, 157-159 and 162-164 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected groups and species, there being no allowable generic or linking claim.

3. Claims 136 and 167-176, insofar as they read upon the elected species, are examined on the merits in this Office action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 136 and 167-176 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 136 and its dependents are rendered indefinite by the recitation of "endothelial cells expressing a carboxylated glycan" in the second line of claim 136 and the subsequent recitation of "providing... a carboxylated glycan" in lines 4-5 of the claim and the recitation of "said carboxylated glycan" in lines 7-8 of the claim. It is unclear which carboxylated glycan "said carboxylated glycan" refers to and it is further unclear whether the two carboxylated glycans recited in line 2 and lines 4-5 are intended to be

the same carboxylated glycan or a different carboxylated glycan. Further, carboxylated glycans are recited throughout the claim and the specific glycan to which these instances refer is not set forth in the claim, leaving one unclear as to whether applicant refers to a single carboxylated glycan or a number of multiple glycans. Claims 167-169 also recite these inconsistencies and it is unclear which carboxylated glycans the specific steps recited in the claims refer to. Therefore, the metes and bounds of the claims would be unclear to one of ordinary skill in the art.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 167-169 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. It is apparent that the antibodies (mAbEE4.1, mAbGB3.1 and mAbEH2.7) recited in the claims are required to practice the claimed invention. As such the biological material must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not obtainable or available, the requirement of 35 USC 112, first paragraph may be satisfied by a deposit of the biological material.

10. The process disclosed in the specification does not appear to be repeatable, it is not clear that the invention will work with commonly available material and it is not apparent if the biological materials are both known and readily available to the public.

11. If a deposit has been made under the terms of the Budapest Treaty, then a statement, affidavit or declaration by applicant, or a statement by an attorney of record over his or her signature and registration number, or someone empowered to make such a statement, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

12. If a deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, applicant may provide assurance of compliance by statement, affidavit or declaration, or by someone empowered to make the same, or by a statement by an attorney of record over his or her signature and registration number showing that:

a. during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;
b. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
c. the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last requires or for the enforceable life of the patent, whichever is longer;
d. a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and
e. the deposit will be replaced if it should ever become inviable.

13. A Statement of Biological Deposit was filed in this application on January 28, 2008. Applicant states that a biological deposit will be made in this application during pendency of the application (i.e., on or before payment of the issue fee). This is

respectfully noted and applicant may choose to delay to deposit the biological material until a time when all other claims in the application are in condition for allowance. Applicant further states, in the remarks filed on October 7, 2009, that a deposit has been made and that the ATCC accession numbers of the biological cells are recited in claims 167-169. However, it is evident that the instant claims do not recite these accession numbers. Since it is unclear whether a biological deposit has in fact been made, the rejection of the claims reciting the biological material stands until the biological deposit is made of record.

14. Claims 136 and 170-176 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a test agent which reduces binding to specific carboxylated glycans, does not reasonably provide enablement for identifying the test agent as reducing inflammation in a tissue comprising endothelial cells expressing said carboxylated glycan. Claim 136 recites a method for identifying a test agent as reducing inflammation in a tissue that comprises endothelial cells expressing a carboxylated glycan, said method comprising: (A) providing: (i) a carboxylated glycan that binds to a first molecule comprising one or more of S100A8, S100A9, S100A12, amphoterin, annexin I, and a polypeptide sequence from amino acids 1 to 12 of annexin I, wherein said carboxylated glycan is purified by a method comprising (a) providing (i) a second molecule comprising a carboxylated glycan; (ii) biotinylated diamino pyridine (BAP); and (iii) an exoglycosidase; (b) conjugating said second molecule to said BAP to produce a BAP-glycan conjugate; (c)

treating said BAP-glycan conjugate with said exoglycosidase to produce a treated BAP-glycan conjugate comprising an anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (d) isolating said anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule, thereby producing a purified carboxylated glycan; (ii) an antibody that specifically binds to said carboxylated glycans, wherein said binding is not reduced by a carboxylate-neutralized glycan; and (iii) a test agent; (B) contacting said purified carboxylated glycan, said antibody, and said test agent; (C) detecting a reduction in the level of binding of said antibody to said purified carboxylated glycan in the presence of said test agent compared to in the absence of said test agent, thereby identifying said test agent as reducing inflammation in a tissue comprising endothelial cells that express said carboxylated glycan. Claims 170 recites the method of claim 136 further comprising (D) administering the test agent to a mouse having inflammation in a tissue comprising endothelial cells that express said carboxylated glycan, and (E) detecting a reduction in said inflammation in the presence of said test agent compared to in the absence of said test agent. Claims 171-176 recite that the first molecule comprises S100A8, S100A9, S100A12, amphoterin, annexin I, or a polypeptide sequence from amino acids 1 to 12 of annexin I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

15. In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230

U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the instant case, those factors deemed most relevant are the quantity of experimentation necessary, the predictability or unpredictability of the art and the breadth of the claims.

16. The disclosure is not enabling for identifying a test agent as reducing inflammation because it does not present enough direction and guidance for one skilled in the art to use the invention with a reasonable expectation of success without undue experimentation. Although the disclosure provides guidance for the identification of some agents which reduce inflammation related to the binding of the proteins annexin I, S100A8/A9 and amphoterin, the disclosure does not provide any guidance or working examples to direct one to the development of a screening method that would identify any test agent that reduces inflammation. Specifically, claim 136 recites a method for detecting a test agent as reducing inflammation in a tissue. However, the method is directed to the discovery of a test agent that may or may not reduce inflammation in a tissue upon further investigation. The identification of an agent that reduces inflammation in vitro may not adequately predict the effect of the agent when used in a patient in vivo. One of ordinary skill in the art would conclude that the agent would

further need to be assessed for its ability to reduce inflammation in a tissue, requiring further and undue experimentation for one of ordinary skill in the art to use the invention as claimed. Thus, it is evident that one of ordinary skill in the art would be unable to predict whether the method would work as claimed (i.e., to identify a test agent as reducing inflammation). Regarding claim 170, one of ordinary skill in the art would further be unable to predict whether the method would work as claimed (to enable one to detect a reduction in inflammation) with a reasonable expectation of success because one would have no prior knowledge whether the test agent would result in reducing inflammation. Further, applicant discloses in the specification that a cascade of molecular events is involved in the production of an inflammatory response, particularly in the recruitment of leukocytes (see specification, pp. 1-3). There is no guidance provided to detect agents that reduce inflammation by pathways other than those disclosed. Due to the complexity of molecular events involved in the production of an inflammatory response, one would be unable to predict whether a test agent would reduce inflammation without undue experimentation. Given these facts, one skilled in the art would be unable to predict whether the claimed method for the identification of agents that reduce inflammation could be performed with a reasonable expectation of success.

17. Therefore, the disclosure of the instant application does not enable one skilled in the art to use the invention as claimed.

Claim Rejections - 35 USC § 102

18. Rejections under 35 USC 102 have been withdrawn due to amendment.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 167-169 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varki et al. (US 5,449,781; reference cited in prior action) in view of Hodges et al. (US 5,738,996; reference cited in prior action). The claims recite methods for identifying a test agent as reducing specific binding of a polypeptide to a carboxylated glycan comprising: (A) providing: (i) a carboxylated glycan purified by a method comprising (1) providing (a) a molecule comprising a carboxylated glycan; (b) biotinylated diamino pyridine (BAP); and (c) an exoglycosidase; (2) conjugating said second molecule to said BAP to produce a BAP-glycan conjugate; (3) treating said BAP-glycan conjugate with said exoglycosidase to produce a treated BAP-glycan conjugate comprising an anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule; and (4) isolating said anionic BAP-glycan conjugate having from 1 to 2 negative charges per molecule, thereby producing a purified carboxylated glycan; (ii) an antibody (mAbEE4.1, mAbGB3.1 or mAbEH2.7) that specifically binds to said carboxylated glycans, wherein said binding is not reduced by a carboxylate-neutralized glycan; and (iii) a test agent; (B) contacting said purified carboxylated glycan, said antibody, and said test agent; (C) detecting a reduction in the level of binding of said antibody to said purified carboxylated glycan in the presence of said test agent compared to in the absence of said test agent, thereby identifying said test agent as reducing specific binding of a polypeptide to a carboxylated glycan.

23. Varki teaches a method for purifying a carboxylated glycan (e.g. those containing siacylic acid residues) comprising conjugating a carboxylated glycan with BAP; treating the BAP-glycan conjugate with an exoglycosidase (sialidase); and isolating the BAP-

glycan conjugate (by HPLC), thereby purifying the glycan (col. 9, line 51-col. 10, line 8, col. 10, lines 47-62). Although Varki does not specifically teach that the BAP-glycan conjugate has 1-2 negative charges per molecule, the process may use a number of conjugates that would inherently have the claimed charges. Varki teaches a method for screening recombinant protein libraries using the BAP-conjugated glycans to identify proteins that bind to the saccharides (col. 7, lines 17-25). Varki teaches that IgG antibodies can be produced which specifically bind to the purified glycans (col. 7. lines 8-13).

24. Varki does not specifically teach a method for identifying a test agent that reduces specific binding of a polypeptide to a carboxylated glycan, and does not teach the specific antibodies recited in the claims.

25. Hodges teaches a test method wherein a labeled antigen, which may be immobilized, is bound to an antibody and a test agent, wherein the reduction of the level of binding of the antibody to the antigen is detected and is indicative of specific binding of the test agent to the antigen (col. 13, lines 28-44, col. 14, lines 6-15).

26. At the time of the invention, a method for purifying a carboxylated glycan comprising nearly all of the claimed elements was known, as taught by Varki. It was further known at the time of the invention that tests could be conducted to detect the specific binding of a test agent by measuring the reduction in the specific binding of an antibody, as taught by Hodges. One or ordinary skill in the art would have been motivated to combine these teachings because Varki teaches that it would be desirable to use the methods to screen for proteins which bind to the saccharides, and that the

methods enable the production of antibodies specific for the saccharides (col. 7, lines 18-21). Hodges teaches a method using antibodies to screen for proteins that bind to an antigen. One would therefore have recognized that it would be desirable to use the methods of Hodges in combination with the method taught by Varki. Furthermore, it would have been considered a matter of routine experimentation to produce antibodies with desirable characteristics, such as those which bind to saccharides of interest. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because Varki teaches all of the required elements, and Hodges teaches simplified screening methods. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

27. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

28. Applicant's arguments filed October 7, 2009 have been fully considered but they are not persuasive. Applicant argues that the conditions for biological deposit have been fulfilled. However, although applicant states that a deposit has been made and that the ATCC accession numbers of the biological cells are recited in claims 167-169, it is evident that the instant claims do not recite these accession numbers. Since it is unclear whether a biological deposit has in fact been made, the rejection of the claims reciting the biological material stands until the biological deposit is made of record.

29. Applicant also argues that the disclosure of the instant application is fully enabled so as to allow one of ordinary skill in the art to use the invention as claimed. However, as discussed in the rejections above, although the disclosure provides guidance for the identification of some agents which reduce inflammation related to the binding of the proteins annexin I, S100A8/A9 and amphoterin, the disclosure does not provide any guidance or working examples to direct one to the development of a screening method that would identify any test agent that reduces inflammation. The disclosure is directed to the discovery of a test agent that may or may not reduce inflammation in a tissue upon further investigation, which is contrary to the claims, which are directed to the identification of a test agent as reducing inflammation. One of ordinary skill in the art would be unable to predict whether the method would work as claimed. For these reasons and those set forth in the rejections above, applicant's arguments have not been found to be persuasive.

30. Therefore, applicant's arguments have been fully considered, but they have not been found to be persuasive.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN MACAULEY whose telephone number is (571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sue Liu can be reached on (571) 272-5539. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM

/SUE LIU/
Supervisory Patent Examiner, Art Unit 1653